

Linking With Multiple State Cancer Registries for Safety Surveillance Study – Is it Feasible?

Alicia Gilsonan,¹ David Harris,¹ Kirk Midkiff,¹ Jean Wright,² Elizabeth Andrews¹

¹ RTI Health Solutions, Research Triangle Park, NC, United States; ² Eli Lilly and Company, Indianapolis, IN, United States

ABSTRACT

Background: In 2009, the voluntary Forteo Patient Registry was implemented as one method to characterize the possible risk of osteosarcoma in patients taking teriparatide. Patient information will be linked annually for 12 years with state cancer registry data. Due to the individualized approval process for each state, launching a data linkage study with multiple state cancer registries at the same time can be challenging.

Objective: To describe the feasibility of performing a data linkage in the United States with multiple state cancer registries and the Forteo Patient Registry.

Methods: Patients are invited to participate in the Forteo Patient Registry through multiple routes of communication and are registered once a one-page registration form and signed informed consent form are returned. In May 2009, cancer registries in all 50 states and the District of Columbia were invited to participate in the first annual linkage. A database was developed to track the recruitment process. All necessary applications and agreements for study approval were submitted to cancer registries. Registries that completed all local approval requirements and attended training on a standard linkage algorithm developed for this study were included in the first annual linkage in September 2010.

Results: Forty-two of 51 cancer registries expressed interest in participating. Of these 42 registries, 28 required local institutional review board (IRB) approval and 14 deferred to the central IRB. At least one additional approval was required at 36 of the 42 registries. Twenty-seven registries met all approval requirements in time to participate in the first annual data linkage. The average time from submission of the first application to the date that all necessary approvals and agreements were in place was 94 days (range, 10-195 days). These registries (covering 70% of the adult United States population) were successful in using the standard linkage algorithm.

Conclusions: Although there are substantial challenges in conducting a data linkage with multiple state cancer registries, including developing a customized recruitment strategy for each cancer registry, the results of the first linkage indicate that it is feasible.

INTRODUCTION

- Teriparatide (Forteo) was initially approved in 2002 in the United States (US) for treatment of postmenopausal women with osteoporosis and for men with low bone mineral density at high risk for bone fractures.
- In rat toxicology studies, teriparatide caused increases in bone mass and a dose-dependent increase in the incidence of osteosarcoma.¹
- In July 2009, as a condition of approval of a new indication for Forteo, the FDA required the implementation of a voluntary, prospective registry to estimate the incidence of osteosarcoma in patients receiving treatment with Forteo. A prospective study of Forteo users and linkage with cancer registries was designed for the following reasons:
 - Despite the availability of large health care databases for studies of acute adverse effects of medications, no existing source exists for capturing rare events.
 - Cancer registries offer a primary source for comprehensive and accurate capture of all cases of tumors such as osteosarcoma.

- Adult patients (aged 18 years and older) are invited to participate in the registry through a variety of methods. Participation involves providing signed consent and a small amount of data at the time of enrollment. No further contact is made with the participants.
- The study requires a large sample size of Forteo users from across the US and participation by a large percentage of US cancer registries, because adult osteosarcoma is rare (2.7 cases per million persons per year).² The goal for the first year was to link with a minimum of 25 state cancer registries.
- In order to achieve the goal for state cancer registry participation, a structured registry recruitment plan, linkage algorithm, and training program were put in place.
- The study has been approved by the RTI Institutional Review Board (IRB), which serves as the primary IRB for the Forteo Patient Registry and as the central IRB for state cancer registries that can defer to a central IRB.

AIM

- The aim for this poster is to describe the results of the structured approach for registry recruitment and the first linkage of this safety surveillance study.

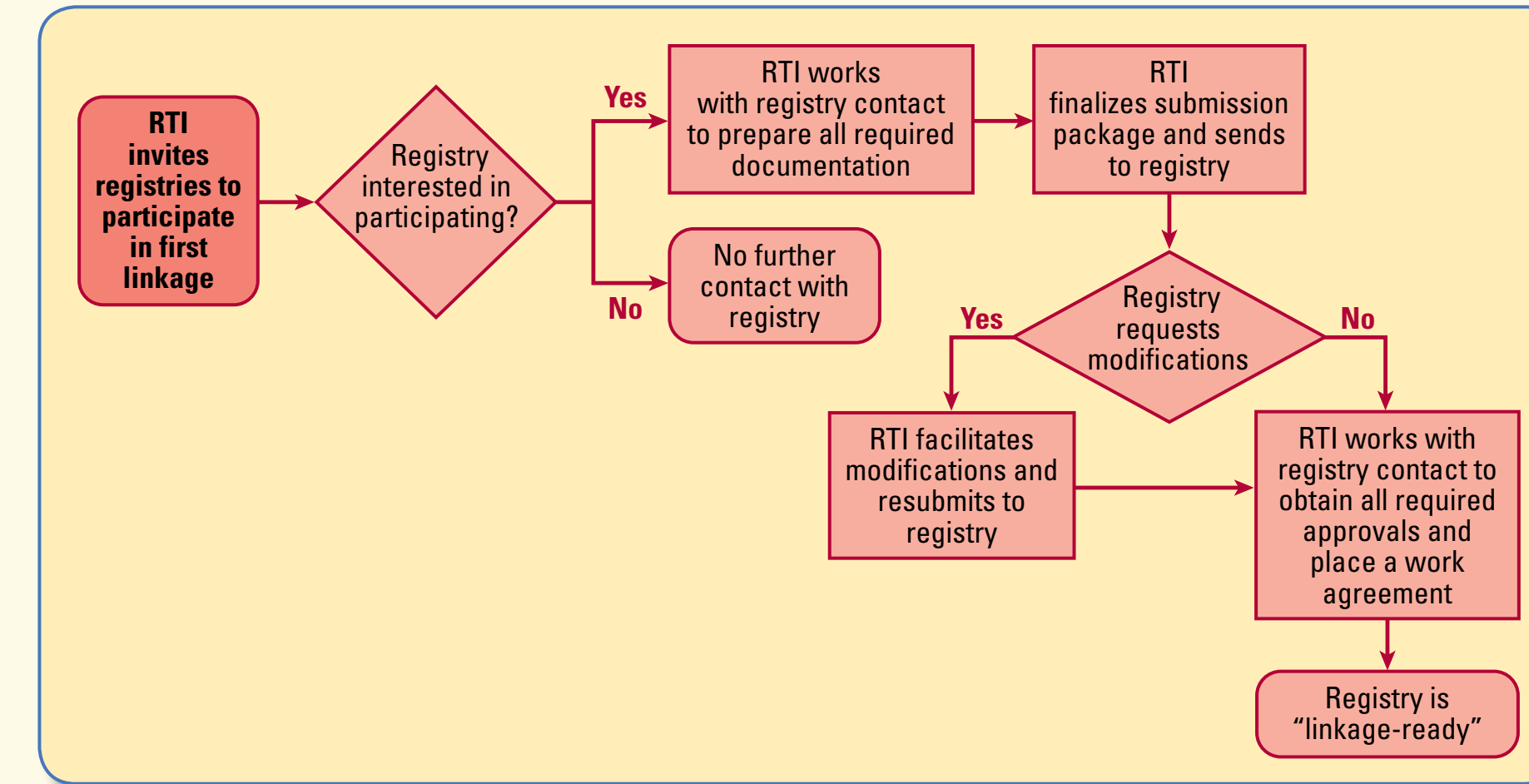
METHODS

Registry Recruitment

- Cancer registries in all 50 states and the District of Columbia were invited to participate by RTI in May 2009.
- States that expressed interest were contacted, and their specific requirements for study approval were assessed.
- The recruitment process was tracked using a database designed for this purpose.
- RTI developed standardized text for responses anticipated by the IRB and privacy requirements for use in the application process for individual registries.
- All necessary applications and agreements for study approval, including ethics and data use agreements, were submitted to individual state cancer registries.
- States were considered “linkage-ready” once all required approvals were obtained and a work agreement was established.

Figure 1 shows the planned approach to cancer registry recruitment.

Figure 1. Registry Recruitment Plan



Linkage

- Cancer registries were trained to use a standard linkage algorithm created and tested by RTI International³ in collaboration with three registries that reviewed the algorithm and procedures.
- Link Plus (v2.0), a probabilistic matching software program available from the Centers for Disease Control and Prevention, was used to develop the algorithm.
- Link Plus was selected because it was designed specifically for linking with state cancer registry data, is easy to use, and is readily accessible.
- Registration data (Figure 2) from eligible patients enrolled in the study as of July 26, 2010, were sent to participating state cancer registries via a secure FTP.
- Registries used a standardized form to document results of the linkage, including the number of osteosarcoma cases in their database and whether any matched with the Forteo registry participants provided by RTI.

Figure 2. Forteo Patient Registry Registration Data

CONCLUSIONS

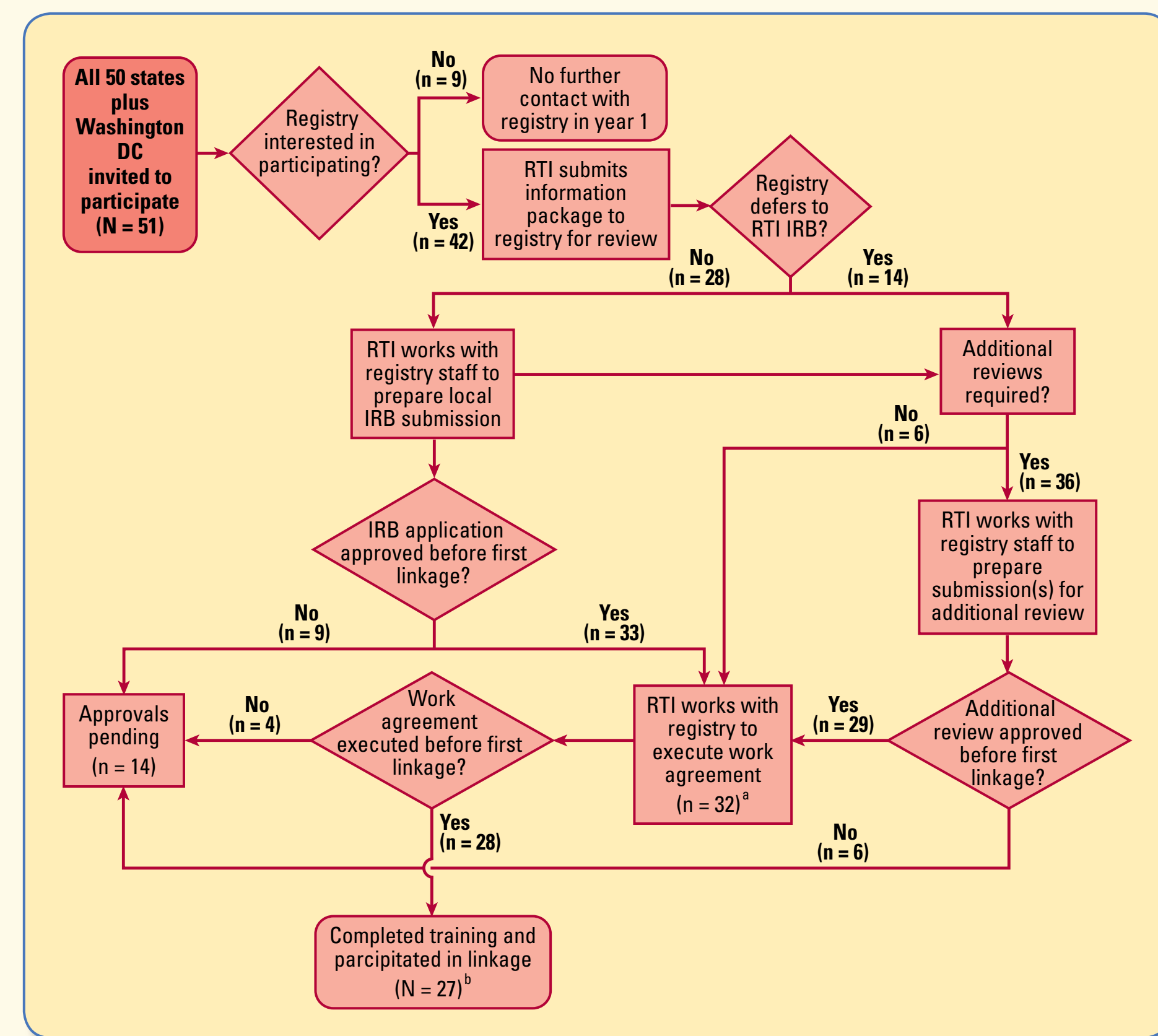
- The results of the first linkage with Forteo Patient Registry data indicate that it is feasible for a large number of states to perform a data linkage concurrently, using a standard data linkage algorithm.
- There are substantial challenges in obtaining approvals to conduct a study with many state cancer registries, because the same core information package detailing the study design, methods, and human subjects protections must be customized for many different review committees, using unique review criteria.
- Effective communication and collaboration between the researcher and cancer registry is essential for successfully navigating the variety of review and approval requirements that may evolve over time.
- A standardized research application and approval process for all state cancer registries would be extremely helpful to researchers and registries that wish to collaborate on similar studies, furthering our knowledge about the long-term safety of medications.

Lessons Learned

- Population-based studies that use data from state cancer registries play a significant role in drug safety surveillance activities. The opportunity for further collaboration is high, paralleling the public and regulatory interest in the long-term risk of cancer associated with many new therapies.
- In the absence of a national cancer registry with patient-level identifying data in the US, many studies will require participation of multiple statewide cancer registries.

RESULTS

Figure 3. RTI Composite Experience for Registry Recruitment as of September 2010

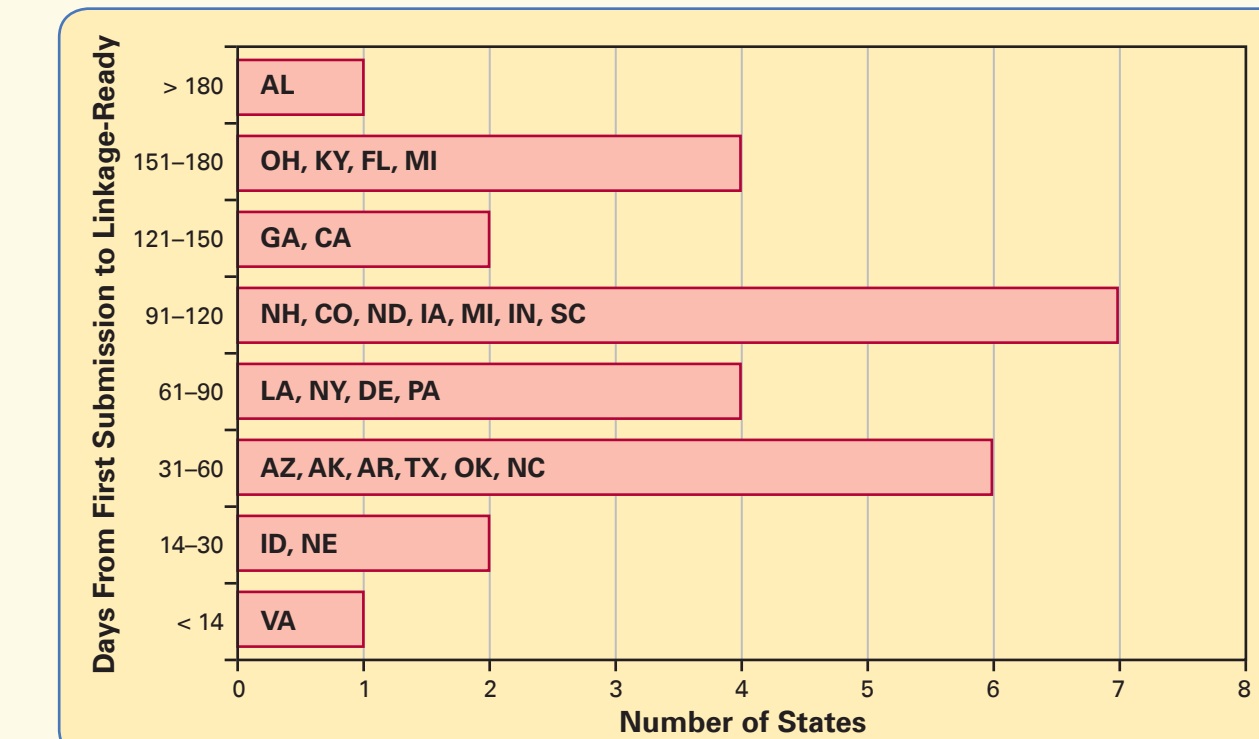


^a IRB approval and additional review approved are not mutually exclusive; therefore, number moving to work agreement is less than sum of those two boxes.
^b One registry was not able to participate in the linkage due to resource constraints.

Registry Recruitment

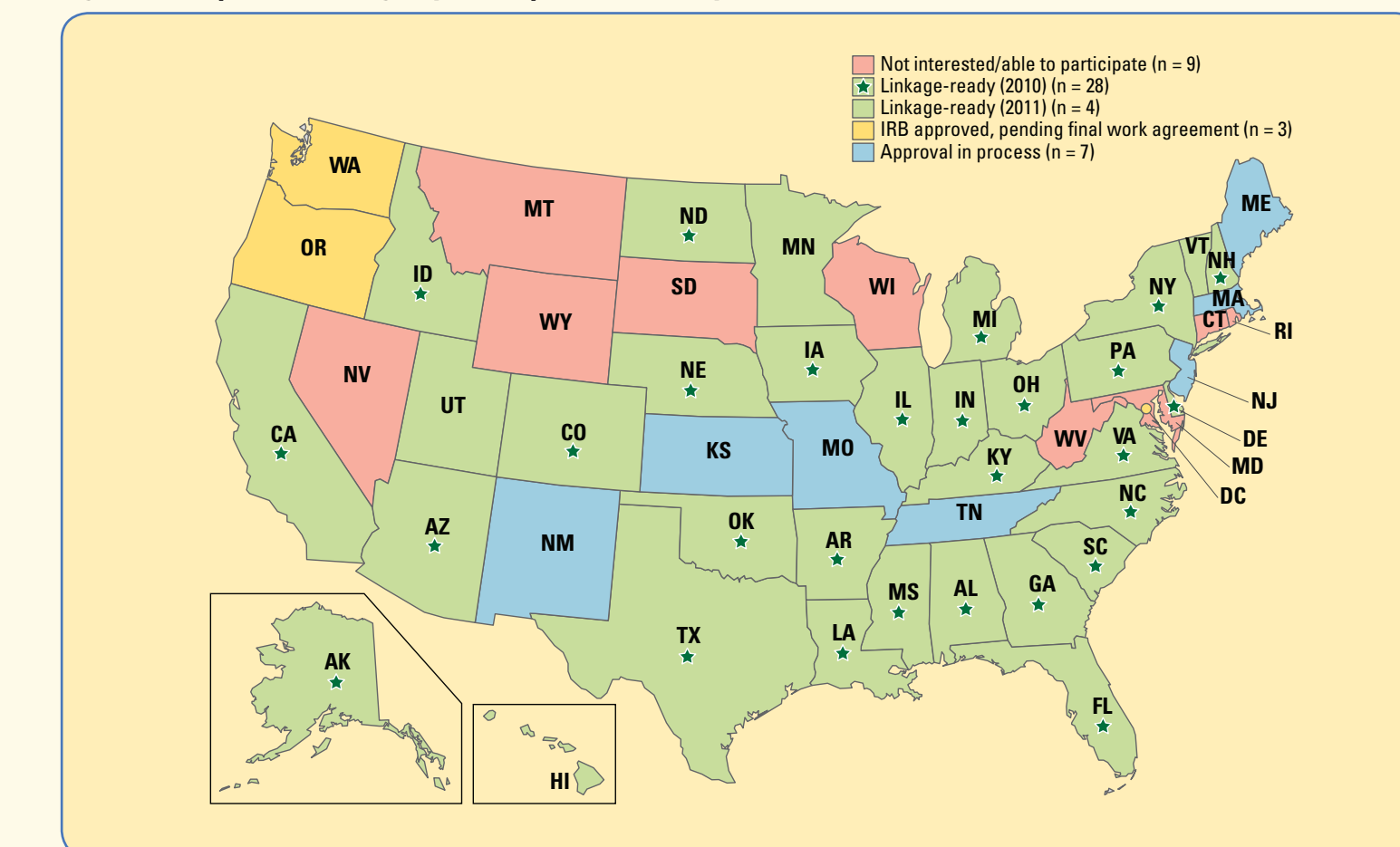
- All 50 states plus the District of Columbia were invited to participate. Figure 3 describes the results of the initial effort to identify and enroll states interested in participating at the time of the first linkage, September 2010.
- The understanding of study approval requirements locally by the registries and RTI evolved over time (from the initial expression of interest to “linkage-ready” status) and resulted in an iterative process to obtain necessary approvals.
- RTI was able to use the core standardized text for the required registry submissions; however, the level of detail and wording had to be extensively customized, adapted, and reorganized to accommodate the required format specific to each registry.
- 28 states completed all necessary requirements in time for the 2010 linkage. However, one registry was not able to participate in the linkage due to resource constraints.
- The average time from submission of the first application to the date the registry was linkage-ready was 94 days (range: 10 days to 195 days) (Figure 4).

Figure 4. Time From First Submission to Linkage-Ready Status for Cancer Registries That Participated in the 2010 Data Linkage



- Interested registries not able to complete the process before the first linkage continue to work with RTI to complete approvals needed to participate. Figure 5 displays a map of the state cancer registries and their status of participation as of May 15, 2011.

Figure 5. Map of Forteo Registry Participation as of May 15, 2011



Linkage

- In September 2010, the first annual linkage was completed between the Forteo Patient Registry database and cases of osteosarcoma diagnosed since January 1, 2009, from 27 participating state cancer registries (which covered 70% of the adult US population).
 - 6,338 patients from the Forteo Patient Registry were linked with a total of 431 adult osteosarcoma cases.
 - No matches were found.
- Due to the 9- to 18-month lag time between the date of cancer diagnosis and date the case is included in the state cancer registry databases, the osteosarcoma cases included in this first annual linkage are a subset of all osteosarcoma cases diagnosed in 2009 and 2010 in these registries, and additional 2009 and 2010 cases will be included in future linkages.

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DISCLOSURE

This study is sponsored by Eli Lilly and Company. RTI-HS retains independent right to publish.

CONTACT INFORMATION

Alicia Gilsonan,
Senior Director, Epidemiology
RTI Health Solutions
200 Park Offices Drive
Research Triangle Park, NC 27709
Phone: +1.919.541.8745
Fax: +1.919.541.7222
E-mail: agilsonan@rti.org
Presented at: 27th ICPE: International Conference on Pharmacoepidemiology & Therapeutic Risk Management
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